ABSTRACTS – POSTER

1159 Acute Myocardial Infarction: Determinants of Infarct Size and Myocardial Function

Wednesday, April 1, 1998, 9:00 a.m.–11:00 a.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 10:00 a.m.–11:00 a.m.

1159-107 Long-term Effects of Heart Rate Reduction by Zatebradine on Mortality, Hemodynamics and Remodeling in Rats With Experimental Myocardial Infarction

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Background: The mechanism of reduced mortality after infarction (MI) by betablocker is not fully understood. It could be a specific betablocker effect, an effect related to heart rate (HR) reduction or the prevention of left ventricular (LV) remodeling or a combined effects. We examined, therefore, the effects of zatebradine (Z), a specific bradycardic agent, to LV function, diastolic wall stress, remodeling and mortality in rats with various MI sizes.

Methods: Z (100 mg/kg/day) or placebo (P) was given 30 minutes after coronary artery ligation by gavage and continued for 8 weeks. LV systolic (LVSP) and end-diastolic (LVEDP) pressure, HR, dP/dt_{max} were measured by Millar-catheter. LV volume was derived from passive pressure-volume relation. Diastolic wall stress was calculated from LV mass, pressure and volume.

Results: Mortality (30 minutes to 8 weeks) was significantly reduced in Z (46%) vs. P treated rats (66%, $p < 0.05$). HR was reduced, LVSP and dP/dt_{max} remained unchanged and stroke volume index increased in all Z treated rats. LV volume was increased in rats by Z with small MI (2.3 ± 0.1 vs. 1.7 ± 0.1 ml/kg, $p < 0.05$) but remained unchanged in rats with large MI (2.4 ± 0.1 vs. 2.4 ± 0.1 ml/kg, n.s) and similar changes were found in diastolic wall stress after Z treatment.

Conclusion: Present data support the hypothesis that lowering HR per se modulates mortality after acute MI in this rat model. Z treatment promotes LV dilatation in rats with small MI but not in rats with large MI, diastolic wall stress changes might be the underlying causes.

1159-108 Estrogen-Replacement Increases Infarct Size in Ovariectomized Rats

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Background: Estrogen may increase long-term survival of women who have suffered from a myocardial infarction (MI). We examined the acute and chronic influence of estrogen on MI in the rat left coronary artery ligation model.

Methods: Female Sprague Dawley rats aged 12–14 weeks (n = 69) comprising three groups [ovaries intact; ovariectomized and replaced with 17β-estradiol (17β-E_2) or placebo, 2 weeks prior to MI] were randomized to left coronary artery ligation (n = 54) or sham operated (n = 15) groups. 11–12 weeks post-MI, rats were euthanized and left ventricular (LV) function was assessed (Langendorff preparation) after which the hearts were perfusion fixed before sectioning and staining for morphometric analysis (n = 4–6 per group).

Results: Acutely, estrogen was associated with a trend towards increased mortality. Infarct size was increased in the 17β-E_2 group compared to placebo, whereas chronic wall tension was normalized through a reduction in LV cavity size with estrogen treatment (see Table).

	Intact MI	17β-E_2 MI	PlaceboMI
% Acute mortality (≤24 h)	39	47	24
% Infarct size	35 ± 6	42 ± 2††	26 ± 3
Cavity area: septal thickness ratio	14.0 ± 3.5	13.2 ± 0.9†	22.2 ± 5.1
Peak wall tension (mmHg.mm)	474 ± 115	419 ± 41*	946 ± 300
Serum 17β-E_2 (pg/ml)	34 ± 3**	46 ± 9**	17 ± 3

* $P < 0.05$; ** $P < 0.01$; † $P = 0.05$; †† $P = 0.01$ compared to placebo (one-way ANOVA-Bonferroni)

Conclusions: These results suggest that estrogen is detrimental at the time of MI, resulting in an increased size of infarct, but that chronically it can normalize wall tension and inhibit LV dilatation which may in turn lead to increased long-term survival. Possible mechanisms of these estrogenic effects are presently the subject of investigation in our laboratory.

1159-109 Impact of Myocardial Viability on Left Ventricular Dilatation Following Acute Myocardial Infarction

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Background: Dobutamine-responsive wall thickening indicates presence of viable myocardium. Since even a small rim of viable epicardial myocardium may be sufficient to prevent infarct expansion, left ventricular dilatation may occur less in patients with viability after myocardial infarction.

Methods: To test this hypothesis, low-dose dobutamine stress echocardiography was performed in 107 patients 3 ± 1 days after acute myocardial infarction. Myocardial segments were scored at rest and during dobutamine infusion (5–10 ug/kg/min) using a 13-segment model and a 4-grade scoring system. Viability was defined as an improvement of at least 1 grade in ≥2 segments. 2D-echocardiography was repeated 3 months later.

Results: Baseline characteristics were comparable between patients with (n = 47) and without (n = 60) viability. Left ventricular end-diastolic volume index (EDVI) was stable in patients with viability, whereas end-systolic volume index (ESVI) decreased significantly ($P = 0.006$). In contrast, patients without viability showed a significant increase in both EDVI ($P < 0.0001$) and ESVI ($P = 0.0007$). Subgroup analysis in patients with small and large infarctions (peak CK ≤1000 U/L vs >1000 U/L) revealed that ventricular dilatation occurred only in patients with large infarctions, without viability. Multivariate regression analysis identified myocardial viability as independent predictor of left ventricular dilatation.

Conclusions: Presence of viability early after acute myocardial infarction is associated with preservation of left ventricular size, whereas absence of viability results in ventricular dilatation.

1159-110 Nonuniform Relationship Between Infarct Size and Remodeling and Hemodynamic Consequences in Rat

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Background: Although infarct (MI) size is the most important determinant for the left ventricular (LV) dilation and remodeling, individual variability of LV volume to a given MI size is high in patients. We analyzed this nonuniform relationship between MI size and degree of LV dilation and potential hemodynamic consequences in rat with chronic MI.

Methods: Eight weeks post MI or sham operation, LV systolic (LVSP) and end-diastolic (LVEDP) pressure, cardiac index were measured by Millar-catheter or electromagnetic flowmeter, respectively. LV volume (Vol) was derived from passive pressure-volume relation and MI size determined by planimetry. Infarct expansion index (EI) was defined as LV cavity area/total LV area x septum thickness/free wall thickness. Four patterns were predefined by the median of MI size and range of normal LV volume (95% confidential interval of sham): A, small MI + LV dilation; B, small MI without dilation; C, large MI + LV dilation and D, large MI without dilation.

Results:

	A (n = 6)	B (n = 23)	C (n = 18)	D (n = 15)
MI Size (%)	21 ± 3	19 ± 2	47 ± 2	44 ± 2
LVSP (mmHg)	135 ± 4	139 ± 3	120 ± 3	130 ± 4
LVEDP (mmHg)	7.6 ± 2.1	4.8 ± 0.4	20.0 ± 2.9	11.3 ± 2.4†
CI (ml/min/kg)	225 ± 12	221 ± 10	178 ± 8	221 ± 9†
LV Vol (ml/kg)	1.30 ± 0.07	0.71 ± 0.04*	1.52 ± 0.09	0.83 ± 0.04†
EI	2.1 ± 0.5	1.7 ± 0.2	5.8 ± 1.0*	2.6 ± 0.3†

(Mean ± sem; * $p < 0.05$ vs. A, † $p < 0.05$ vs. C)

Conclusion: Nonuniform remodeling develops in 45% of large MI rats with unexpected small LV volume (D) which is due to less MI expansion. LV dysfunction is closer related to LV dilation than to MI size.